Serial No.: 10/501,120 Filed: December 20, 2004

Page 2 of 26

Listing of the Claims

Please amend the claims as follows. This listing of claims will replace all prior versions and listings of claims in the application.

1. **(Previously Presented)** A compound having the structure **(I)**:

$$\begin{array}{c|c}
R_1 \\
R_2 \\
R_3 \\
R_4 \\
\end{array} \begin{array}{c}
(A)_{x(1)_y} \\
(E)_z \\
O \\
O \\
R_5 \\
\end{array} \begin{array}{c}
R_6 \\
N \\
C \\
O \\
R_5 \\
\end{array}$$
(I)

or pharmaceutically acceptable derivative thereof;

wherein each occurrence of A, J, E, D and G is independently CR_A, CR_AR_B, C=O, O, S, NR_A, or N, wherein each occurrence of R_A and R_B is independently hydrogen, a protecting group, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

A and J, J and D, D and E, and D and G are each independently linked by a single or double bond as valency permits;

w, x, y and z are each independently 0, 1, 2, 3, 4, 5 or 6, but the sum of x, y and z is 2-6 and the sum of x and y is 1-6;

 R_1 , R_2 , R_3 and R_4 are each independently hydrogen, halogen, -CN, -OR_C, -SR_C, -NR_CR_D, -(C=O)R_C or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_C and R_D is independently hydrogen, a protecting group, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or R_C and R_D , taken together, form a heteroalicyclic or heteroaryl moiety; or wherein any two adjacent groups R_1 , R_2 , R_3 and R_4 , taken together, form an alicyclic or heteroalicyclic moiety, or an aryl or heteroaryl moiety;

R₅ and R₆ are each independently an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety; and Q is an epoxycarbonyl moiety having the structure:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 3 of 26

wherein R^{Q1} is hydrogen, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, an oxygen protecting group or a prodrug moiety.

2. (Original) The compound of claim 1, wherein the compound has the structure:

$$\begin{array}{c|c} R_1 & & \\ R_2 & & \\ R_3 & & \\ R_4 & & \\ \end{array} \begin{array}{c} (A)_{x(J)_y} & & \\ (E)_z^D & & \\ O & & \\ \end{array} \begin{array}{c} H & O \\ N & \\ R_5 & \\ \end{array} \begin{array}{c} R_6 \\ N \\ R_5 \end{array}$$

- 3-4. (Canceled).
- 5. (Previously Presented) The compound of claim 1, wherein R_5 is $-CH_2OR_{5a}$ and the compound has the structure:

$$R_{2}$$
 R_{3}
 R_{4}
 $(E)_{z}^{D}$
 $(G)_{w}$
 $(E)_{z}^{O}$
 $(G)_{w}$
 $(E)_{z}^{O}$
 $(G)_{w}$
 $(G)_{w}$

wherein R_{5a} is hydrogen, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, an oxygen protecting group or a prodrug moiety.

6. (Previously Presented) The compound of claim 1, wherein R_5 is aryl or heteroaryl and the compound has the structure:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 4 of 26

$$R_{2}$$
 R_{3}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{4}
 R_{5}
 R_{4}
 R_{5}
 R_{6}
 R_{7}
 R_{7

wherein AR is an aryl or heteroaryl moiety.

7. **(Previously Presented)** The compound of claim 1, wherein R_5 is $-CH_2NR_{5a}R_{5b}$ or heteroaryl and the compound has the structure:

$$R_{2}$$
 R_{3}
 R_{4}
 $(E)_{z}$
 $(G)_{w}$
 $(G)_{w}$

wherein R_{5a} and R_{5b} are each independently hydrogen, a nitrogen protecting group, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or a prodrug, or R_{5a} and R_{5b} , taken together, form a heteroalicyclic or heteroaryl moiety.

8-12. (Canceled).

13. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1, and A, J and E are each CH₂ and D is CH.

14-15. (Canceled).

16. (Previously Presented) The compound of claim 1, wherein G is CH₂ and w is 0, 1, or 2.

Serial No.: 10/501,120 Filed: December 20, 2004

Page 5 of 26

- 17. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂; D is CH; G is CH₂ and w is 0, 1, or 2..
- 18. **(Previously Presented)** The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

$$R_{2}$$
 R_{3}
 R_{4}
 $CH_{2})_{w}$
 H
 O
 H
 O
 OH

wherein w is 0, 1 or 2; and R_1 , R_2 , R_3 and R_4 are each independently hydrogen, OR_C , halogen, or NR_CR_D , wherein each occurrence of R_C and R_D is independently hydrogen or lower alkyl.

19. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

$$R_{2}$$
 R_{3}
 R_{4}
 $(CH_{2})_{w}$
 H
 O
 H
 O
 O
 OH

wherein AR is an aryl or heteroaryl moiety; w is 0, 1 or 2; and R_1 , R_2 , R_3 and R_4 are each independently hydrogen, OR_C , halogen, or NR_CR_D , wherein each occurrence of R_C and R_D is independently hydrogen or lower alkyl.

20. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 6 of 26

wherein R_{5a} and R_{5b} are each independently hydrogen, a nitrogen protecting group, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or a prodrug, or R_{5a} and R_{5b} , taken together, form a heteroalicyclic or heteroaryl moiety; w is 0, 1 or 2; and R_1 , R_2 , R_3 and R_4 are each independently hydrogen, OR_C , halogen, or NR_CR_D , wherein each occurrence of R_C and R_D is independently hydrogen or lower alkyl.

21-23. (Canceled).

24. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

$$(R_CO)_q$$
 $(CH_2)_w$ $(CH_2)_w$

wherein w is 0, 1 or 2, each occurrence of R_{C} is independently lower alkyl, and q is 0, 1, 2, 3 or 4.

25. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

$$(R_{c}O)_{q}$$
 $(CH_{2})_{w}$ $(CH_$

Serial No.: 10/501,120 Filed: December 20, 2004

Page 7 of 26

wherein AR is an aryl or heteroaryl moiety; w is 0, 1 or 2, each occurrence of R_C is independently lower alkyl, and q is 0, 1, 2, 3 or 4.

26. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

$$(R_{c}O)_{q}$$
 $(CH_{2})_{w}$ $(CH_$

wherein R_{5a} and R_{5b} are each independently hydrogen, a nitrogen protecting group, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or a prodrug, or R_{5a} and R_{5b} , taken together, form a heteroalicyclic or heteroaryl moiety; w is 0, 1 or 2, each occurrence of R_C is independently lower alkyl, and q is 0, 1, 2, 3 or 4.

27-29. (Canceled).

30. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

$$(MeO)_{q}$$
 $(CH_2)_{w}$ $(CH_$

wherein w is 0, 1 or 2; and q is 0, 1, 2, 3 or 4.

31. (Previously Presented) The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 8 of 26

$$(MeO)_q$$
 $(CH_2)_w$ $(CH_2)_w$

wherein AR is an aryl or heteroaryl moiety; w is 0, 1 or 2; and q is 0, 1, 2, 3 or 4.

32. **(Previously Presented)** The compound of claim 1, wherein x, y and z are each 1; A, J and E are each CH₂, D is CH and the compound has the structure:

wherein R_{5a} and R_{5b} are each independently hydrogen, a nitrogen protecting group, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or a prodrug, or R_{5a} and R_{5b} , taken together, form a heteroalicyclic or heteroaryl moiety; w is 0, 1 or 2; and q is 0, 1, 2, 3 or 4.

33-37. (Canceled).

- 38. **(Previously Presented)** The compound of any one of claims 1, 2 or 5-7, wherein x, y and z are each 1 and A-J-D-E together represent –CH₂CH₂CH-CH₂–.
- 39. **(Previously Presented)** The compound of any one of claims 1, 2 or 5-7, wherein x is 0, y and z are each 1 and J-D-E together represent -CH₂-CH-CH₂-.

Serial No.: 10/501,120 Filed: December 20, 2004

Page 9 of 26

- 40. **(Previously Presented)** The compound of any one of claims 1, 2 or 5-7, wherein x is 0, z is 0 and E is absent and J-D together represents -CH₂-CH₂-.
- 41. **(Previously Presented)** The compound of any one of claims 1, 2 or 5-7, wherein x, y and z are each 1 and A-J-D-E together represent –N=CH-C=N-.
- 42. **(Previously Presented)** The compound of any one of claims 1, 2 or 5-7, wherein x, y and z are each 1 and A-J-D-E together represent -CH₂CH₂CH-CH₂- and G is CH₂ and w is 0, 1 or 2.
- 43. **(Previously Presented)** The compound of claim 1, wherein R₁, R₂, R₃ and R₄ are each independently hydrogen, halogen, protected or unprotected hydroxyl, protected or unprotected thiol, protected or unprotected amino, alkyl, alkoxy, thioalkyl, mono-or disubstituted alkylamino, or wherein any two adjacent groups R₁, R₂, R₃ or R₄, taken together are a cycloalkyl, heterocycloalkyl, aryl or heteroaryl moiety,

whereby each of the alkyl moieties is independently substituted or unsubstituted, linear or branched, cyclic or acyclic, and each of the aryl and heteroaryl moieties is independently substituted or unsubstituted.

- 44. (Previously Presented) The compound of claim 1, wherein R_1 , R_2 , R_3 and R_4 are each independently hydrogen or lower alkoxy.
- 45. **(Previously Presented)** The compound of claim 1, wherein R_1 , R_2 , R_3 and R_4 are each independently hydrogen or methoxy.
- 46. (Previously Presented) The compound of claim 1, wherein R_1 , R_2 , R_3 and R_4 are each methoxy.
- 47. (Previously Presented) The compound of claim 1, wherein R_1 is hydrogen and each of R_2 , R_3 and R_4 are independently lower alkoxy.

Serial No.: 10/501,120 Filed: December 20, 2004

Page 10 of 26

- 48. (Previously Presented) The compound of claim 1, wherein R_1 is hydrogen and each of R_2 , R_3 and R_4 are methoxy.
- 49. **(Previously Presented)** The compound of claim 1, wherein R_5 is alkyl, cycloalkyl, alkenyl, cycloalkenyl, cycloalkynyl, $C_{1-6}OR_{5a}$, $C_{1-6}NR_{5a}R_{5b}$, aryl or heteroaryl; wherein R_{5a} and R_{5b} are each independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, $-C(NH_2)=N(NO_2)$, $-C(=O)OR_{5c}$, $-C(=O)R_{5c}$ or a protecting group; wherein R_{5c} is hydrogen, alkyl, alkenyl, alkynyl, aryl or heteroaryl.
- 50. **(Previously Presented)** The compound of claim 1, wherein R_5 is alkyl, cycloalkyl, - CH_2OR_{5a} , - $CH_2NR_{5a}R_{5b}$, - CH_2 aryl or - CH_2 heteroaryl; wherein R_{5a} and R_{5b} are each independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, - $C(NH_2)=N(NO_2)$, - $C(=O)OR_{5c}$, - $C(=O)R_{5c}$ or a protecting group; wherein R_{5c} is hydrogen, alkyl, alkenyl, aryl or heteroaryl.
- 51. **(Previously Presented)** The compound of claim 1, wherein R_5 is alkyl, cycloalkyl, CH_2OR_{5a} , $CH_2NR_{5a}R_{5b}$ or substituted or unsubstituted - CH_2Ph ; wherein R_{5a} and R_{5b} are each independently hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, heteroaryl, - $C(NH_2)=N(NO_2)$, - $C(=O)OR_{5c}$, - $C(=O)R_{5c}$ or a protecting group; wherein R_{5c} is hydrogen, alkyl, alkenyl, aryl or heteroaryl.
- 52. (Previously Presented) The compound of claim 1, wherein R₅ is -CH₂OH or benzyl.
- 53. (Previously Presented) The compound of claim 1, wherein R₆ is alkyl, cycloalkyl, alkenyl, cycloalkynyl, aryl or heteroaryl.
- 54. (Previously Presented) The compound of claim 1, wherein R_6 is lower alkyl or aryl.
- 55. (Previously Presented) The compound of claim 1, wherein R_6 is $-CH_2CH(CH_3)_2$.
- 56. (Canceled).

Serial No.: 10/501,120 Filed: December 20, 2004

Page 11 of 26

57. (Previously Presented) The compound of claim 1 or 2, wherein Q has the structure:

58. (Previously Presented) The compound of claim 57, wherein Q has the structure:

59-62. (Canceled).

63. (Previously Presented) A pharmaceutical composition comprising a compound of claim 1; and

a pharmaceutically acceptable carrier or diluent, and optionally further comprising an additional therapeutic agent.

- 64. **(Original)** The pharmaceutical of claim 63 wherein the compound is present in an amount effective to exert an antiproliferative and/or anticancer effect.
- 65. (Original) The pharmaceutical of claim 63 wherein the compound and the additional therapeutic agent are present in an amount effective to exert an antiproliferative and/or anticancer effect.
- 66. (Original) The pharmaceutical of claim 63 wherein the compound is present in an amount effective to exert an anti-inflammatory effect.
- 67. (Original) The pharmaceutical of claim 63 wherein the compound and the additional therapeutic agent are present in an amount effective to exert an anti-inflammatory effect.

Serial No.: 10/501,120 Filed: December 20, 2004

Page 12 of 26

68. (Previously Presented) A method for treating cancer comprising:

administering to a subject in need thereof a therapeutically effective amount of a compound of claim 1; and

optionally further administering an additional therapeutic agent.

- 69. **(Original)** The method of claim 68, wherein the method is used to treat prostate, breast, colon, bladder, cervical, skin, testicular, kidney, ovarian, stomach, brain, liver, pancreatic or esophageal cancer or lymphoma, leukemia, or multiple myeloma.
- 70. (Original) The method of claim 68, wherein the cancer is a solid tumor.

71-80. (Canceled).

81. **(Previously Presented)** The compound of claim 2, wherein Q is a moiety having the structure:

82. (Previously Presented) The compound of claim 81, wherein Q is a moiety having the structure:

83. (Previously Presented) A compound having the structure:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 13 of 26

or pharmaceutically acceptable derivative thereof;

wherein each occurrence of J, D and G is independently CR_A, CR_AR_B, C=O, O, S, NR_A, or N, wherein each occurrence of R_A and R_B is independently hydrogen, a protecting group, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety;

J and D, and D and G are each independently linked by a single or double bond as valency permits;

w is independently 0, 1, 2, 3, 4, 5 or 6,

 R_1 , R_2 , R_3 and R_4 are each independently hydrogen, halogen, -CN, -OR_C, -SR_C, -NR_CR_D, -(C=O)R_C or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, wherein each occurrence of R_C and R_D is independently hydrogen, a protecting group, or an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, or R_C and R_D , taken together, form a heteroalicyclic or heteroaryl moiety; or wherein any two adjacent groups R_1 , R_2 , R_3 and R_4 , taken together, form an alicyclic or heteroalicyclic moiety, or an aryl or heteroaryl moiety;

R₅ and R₆ are each independently an aliphatic, alicyclic, heteroaliphatic, heteroaliphatic, aryl or heteroaryl moiety; and Q is an epoxycarbonyl moiety having the

wherein R^{Q1} is hydrogen, an aliphatic, alicyclic, heteroaliphatic, heteroalicyclic, aryl or heteroaryl moiety, an oxygen protecting group or a prodrug moiety.

84. (Previously Presented) The compound of claim 83, wherein J is CH₂ and D is CH.

85-87. (Canceled)

88. (New) The compound of claim 83, wherein the compound is:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 14 of 26

89. **(New)** The compound of claim 1, wherein the compound is selected from the group consisting of the following compounds:

Serial No.: 10/501,120 Filed: December 20, 2004

Page 15 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 16 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 17 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 18 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 19 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 20 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 21 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 22 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 23 of 26

Serial No.: 10/501,120 Filed: December 20, 2004

Page 24 of 26

90. **(Previously Presented)** The compound of claim 89, wherein the compound is selected from the group consisting of the following compounds: